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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,328	04/25/2005	Klaus Cichutek	GRUND-101	6255
2387	7590	01/15/2008		
Olson & Cepuritis, LTD. 20 NORTH WACKER DRIVE 36TH FLOOR CHICAGO, IL 60606			EXAMINER MARVICH, MARIA	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 01/15/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/510,328	Applicant(s) CICHUTEK ET AL.	
	Examiner Maria B. Marvich, PhD	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 5-9, 11-15, 18 and 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5-9, 11-15, 18 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10/18/07 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f):
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
- 1. ☐ Certified copies of the priority documents have been received.
  - 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1, 2, 5-9, 11-15, 18 and 19 are pending in this application. This office action is in response to an amendment filed 10/18/07.

#### ***Claim Objections***

Claims 1, 9 and 14 are objected to because of the following informalities: in claim 1, the recitation that the "vector comprises a SIVsmmPBj14 virus" should be drawn to a vector comprising --a SIVsmmPBj14 genome--. It is clear that by vector, applicants mean a particle but this is often referred to as a virus and thus it appears that the virus comprises a virus. Claim 9 is objected to because the recitation "pseudotype vectors" sounds as if it is an action required of the method, it would be clearer to recite --pseudotyped vectors--. As well in claim 9, step b) the recitation "expression construct for a non-SIVsmmPBj14 envelope protein" would be clearer if recited as "expression construct comprising the coding sequence of a non-SIVsmmPBj14 envelope protein--. In this way the requirement that the construct comprises the sequences is clearer. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 8 recites "the envelope protein". However, there are two envelope proteins encompassed by the claims that from SIVsmmmPBj15 and the other from the group recited in claim 7. It is unclear to which of these two recitations the claims refer.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pseudotyped in which the SIVsmmPBj14 virus envelope gene is deleted such that the env protein and replaced with an envelope protein from a non SIVsmmPBj14 virus, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This is a new rejection.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The instant claims are drawn to a retrovirus or SIVsmmPBj14 virus comprising a deletion in the *env* gene such that it is non-functional wherein the virus is capable of transducing cells in a G<sub>0</sub> phase as well as cell in the G<sub>1</sub> phase. As well, claims 6-8 are drawn to a pseudotyped vector in which envelope protein of the virus is replaced with that from an alternative species and in claims 9 and 11-15 to a method of making the pseudotyped virus. Claims 18 and 19 are drawn to a lentivirus comprising a SIVsmmmPBj1.9 lentivirus comprising an inactive *env* gene wherein the virus is capable of transducing cells in a G<sub>0</sub> phase. The vectors are broad in that the *env* gene must comprise enough of a deletion such that it is non-functional or must simply be inactive. In the case that the gene is inactive, this appears to suggest that the gene is not expressed which typically does not change the structural characteristics of the gene but is a result of conditions that render the gene inactive. The instant invention is directed toward construction of vectors for transfer of genes into cells in resting G<sub>0</sub> phase wherein the tropism of the virus is altered by alteration of the *env* gene.

The specification teaches that SIVsmmPBj14 viruses are part of the subgroup of lentivirus, which form the larger group of retrovirus. They were isolated from Sooty Mangabey

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monkeys and were found to be capable of replicating in non-stimulated primary human lymphocytes in the  $G_0$  phase. Applicants have determined that the vector does not require the presence of its own *env* gene. Applicants delete SIVsmmPBj14 of internal sequences resulting in its "inactivation". It appears that the gene is considered inactive once protein expression from this region occurs is lost whereas other gene products are produced as they are unaffected by the deletion. However by recitation in the claims that the *env* gene is non-functional or inactive and the VSV *env* gene is active, applicants claim a much broader set of conditions. An active gene appears to only require that the gene is expressed at that time and an inactive gene not expressed for example by use of a promoter that is induced for activated states and un-induced for inactivated states. A functional protein is a protein that is produced but has lost some function. For example in the case of the SIVsmmPBj14 *env* protein, the protein is produced but lacks at least one function such as methylation or phosphorylation or doesn't form a capsid. However, applicants only teach deletions that result in loss of *env* gene expression and not what deletions might affect the protein once expressed to provide a function. The claims do not require that the protein is not expressed or that the protein is not produced.

Secondly, applicants have generated a recombinant SIVsmmPBj14 virus comprising a VSV-G *env* protein and tested the ability of this vector to infect a variety of human cell lines arrested at  $G_0$  and  $G_1$ . Such a virus comprises the entirety of an alternative *env* gene. Applicants demonstrate that these viruses can transducer both with greater efficiency than MLV or HIV. However, applicants do not teach a virus in which the *env* protein is a chimeric as allowed by the claims. For example, the recitation in claim 6 is that only **a part** of an *env* protein from a virus other than SIVsmmPBj14. It is not clear how parts of an *env* protein from a virus other than

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SIVsmmPBj14 can be used in the instant invention particularly given the lack of guidance as to those parts that will lead to a recombinant particle with the ability to transduce cells. This requires an entire *env* gene from a source. The claims and specification are not drawn to a virus with a chimeric envelope protein and such a disclosure would require those details such that a person of skill in the art would not what "parts" must be from SIVsmmPBj14 and what "parts" can be from the second virus.

The invention recites use of a broad genus of viruses. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of viruses derived from SIVsmmPBj14 virus as well as *env* deletions for pseudotyping, the lack of adequate working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Maria B Marvich, PhD  
Examiner  
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